

# Stem Cell Mobilization, Collection, and Processing

Katharina Kriegsmann<sup>a</sup> Patrick Wuchter<sup>b</sup>

<sup>a</sup>Laborarztpraxis Rhein-Main MVZ GbR, Frankfurt am Main, Germany; <sup>b</sup>Institute of Transfusion Medicine and Immunology, Medical Faculty Mannheim, Heidelberg University; German Red Cross Blood Service Baden-Württemberg – Hessen, Mannheim, Germany

Dear Editor,

Mobilizing hematopoietic stem and progenitor cells from the bone marrow into the peripheral blood, collecting them sufficiently by leukapheresis, and transplanting them in an allogeneic or autologous setting as “stem cell graft” is a routine procedure in collection facilities such as in many blood transfusion establishments and transplant centers worldwide. Patients with multiple myeloma and malignant lymphoma are the main candidates for an autologous stem cell transplantation. Today’s induction regimen in both entities have been improved significantly over the last two decades, but the application of high-dose chemotherapy followed by autologous stem cell rescue still represents an essential part of the therapeutic regimen. In this context, the collection of an optimal stem cell product is an important prerequisite.

This special issue of *Transfusion Medicine and Hemotherapy* provides a detailed insight into state-of-the-art stem cell mobilization, collection, and processing techniques. Regarding patients with multiple myeloma, Jantunen et al. comprehensively analyzed current mobilization strategies [1]. The impact of clinical parameters and induction regimens on peripheral blood stem cell (PBSC) mobilization in a large cohort of multiple myeloma patients has been evaluated by Sauer and colleagues [2]. In a more specific approach, Sauer et al. [3] assessed in a second study the effectiveness of autologous stem cell collection after daratumumab-VTD versus VCD. For the entity of mantle cell lymphoma, Turunen et al. examined the cellular composition and the clinical outcome after autologous transplantation [4].

In general, more than 80% of patients succeed in collecting an autologous PBSC graft. However, 10–20% mobilize insufficiently and are so-called “poor mobilizer” [5], but a harmonized definition has not been found yet. Strategies to overcome this problem include the application of plerixafor, either used preemptively or as a rescue strategy [6, 7].

However, comprehensive information on poor mobilizing patients regarding incidence, current treatments, and mobilization strategies is lacking. The German prospective, multicenter, open-label, non-interventional OPTIMOB study addressed this lack of knowledge by analyzing mobilization and collection parameters in a large cohort of adult, transplant-eligible, good and poor mobilizing patients with lymphoma or multiple myeloma. In this special issue, the results of this huge national study with 28 recruiting study centers are presented in two articles: Bittrich et al. [8] described the results in patients with multiple myeloma, whereas Kriegsmann et al. [9] showed the results of the cohort of lymphoma patients.

A state-of-the-art collection of PBSCs includes a system of quality control and benchmarking. Approaches to quantitatively assess the effectiveness of autologous leukapheresis sessions have been developed, and some allow not only to calculate the collection efficiency (CE2) but also to manage the duration of the apheresis session [10–12]. While  $2.0 \times 10^6$  CD34<sup>+</sup> cells/kg body weight (bw) is uniformly accepted as minimum for one autologous transplant, the question of whether more cells for a second or third transplantation or a mere “backup” transplant should be provided is handled divergent. In the allogeneic setting, clinical aspects of both the donor and the recipient have to be considered, e.g., bw differences.

Kayser et al. [13] analyzed a formula, alongside other parameters, to predict the outcome of hematopoietic stem cell collection in healthy allogeneic donors. As the number of requested CD34+ cells may vary between 4.0 and over  $8.0 \times 10^6$  CD34+ cells/kg bw (i.e., if the transplant will be further processed), this approach may help streamline the apheresis session and reduce the burden for the donor.

For decades, CD34 is the decisive marker for enumeration of PBSC grafts, but efforts have been made to develop further marker combinations for a more comprehensive assessment of the graft composition and hence quality (e.g., tri-lineage engraftment). As a step in this direction, Heuer et al. analyzed PBSC subpopulations by flow cytometry and correlated them with clinical outcome after autologous transplantation [14]. Taken together, this special issue of *Transfusion*

*Medicine and Hemotherapy* gives an overview on some of the currently most relevant issues related to procuring PBSC grafts.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Funding Sources

There is no funding related to this article.

### Author Contributions

K.K. and P.W. wrote the manuscript.

## References

- 1 Jantunen E, Partanen A, Turunen A, Varmavuo V, Silvennoinen R. Mobilization strategies in myeloma patients intended for autologous hematopoietic cell transplantation. *Transfus Med Hemother*. 2023. DOI: 10.1159/000531940.
- 2 Sauer S, Hieke L, Brandt J, Müller-Tidow C, Schmitt A, Kauer J, et al. Impact of clinical parameters and induction regimens on peripheral blood stem-cell mobilization and collection in multiple myeloma patients. *Transfus Med Hemother*. 2023. DOI: 10.1159/000530056.
- 3 Sauer S, Kriegsmann K, Nientiedt C, Schmitt A, Müller-Tidow C, Raab M-S, et al. Autologous stem cell collection after daratumumab, bortezomib, thalidomide, and dexamethasone versus bortezomib, cyclophosphamide, and dexamethasone in newly diagnosed multiple myeloma. *Transfus Med Hemother*. 2023. DOI: 10.1159/000529691.
- 4 Turunen AS, Kuittinen O, Kuitunen H, Vasala K, Penttilä K, Harmanen M, et al. CD34+ cell mobilization, autograft cellular composition and outcome in mantle cell lymphoma patients. *Transfus Med Hemother*. 2023. DOI: 10.1159/000531799.
- 5 Wuchter P, Ran D, Bruckner T, Schmitt T, Witzens-Harig M, Neben K, et al. Poor mobilization of hematopoietic stem cells: definitions, incidence, risk factors and impact on outcome of autologous transplantation. *Biol Blood Marrow Transplant*. 2010 Apr;16(4):490–9.
- 6 Cheng J, Schmitt M, Wuchter P, Buss EC, Witzens-Harig M, Neben K, et al. Plerixafor is effective given either preemptively or as a rescue strategy in poor stem cell mobilizing patients with multiple myeloma. *Transfusion*. 2015 Feb;55(2):275–83.
- 7 Hundemer M, Engelhardt M, Bruckner T, Kraeker S, Schmitt A, Sauer S, et al. Rescue stem cell mobilization with plerixafor economizes leukapheresis in patients with multiple myeloma. *J Clin Apher*. 2014 Dec;29(6):299–304.
- 8 Bittrich M, Kriegsmann K, Tietze-Stolley C, Movassaghi K, Grube M, Vucinic V, et al. A German-wide systematic study on mobilization and collection of hematopoietic stem cells in poor mobilizer patients with multiple myeloma prior to autologous stem cell transplantation. *Transfus Med Hemother*. 2023. DOI: 10.1159/000531935.
- 9 Kriegsmann K, Bittrich M, Sauer S, Tietze-Stolley C, Movassaghi K, Grube M, et al. Mobilization and hematopoietic stem cell collection in poor mobilizing patients with lymphoma: Final results of the German OPTIMOB study. *Transfus Med Hemother*. 2023. DOI: 10.1159/000531936.
- 10 Rosenbaum ER, O’Connell B, Cottler-Fox M. Validation of a formula for predicting daily CD34(+) cell collection by leukapheresis. *Cytotherapy*. 2012 Apr;14(4):461–6.
- 11 Cousins AF, Sinclair JE, Alcorn MJ, H A Green R, Douglas KW. HPC: a dose prediction on the optia® cell separator based on a benchmark CE2 collection efficiency: promoting clinical efficiency, minimizing toxicity, and allowing quality control. *J Clin Apher*. 2015;30(6):321–8.
- 12 Lisenko K, Pavel P, Bruckner T, Puthenparambil J, Hundemer M, Schmitt A, et al. Comparison between intermittent and continuous Spectra Optia leukapheresis systems for autologous peripheral blood stem cell collection. *J Clin Apher*. 2017 Feb;32(1):27–34.
- 13 Kayser S, Schlenk RF, Steiner M, Klüter H, Wuchter P. Predicting successful hematopoietic stem cell collection in healthy allogeneic donors. *Transfus Med Hemother*. 2023. DOI: 10.1159/000531236.
- 14 Heuer A, Löwhagen S, Uhlig S, Hetjens S, Büttner S, Pflästerer B, et al. Flow cytometric characterization of HSPC subpopulations in autologous PBSC preparations after cryopreservation. *Transfus Med Hemother*. 2023. DOI: 10.1159/000533624.